UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,552	02/21/2001	Serge Braun	032751-053	5627

21839 7590 01/15/2002

BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
PURI, BEENA	

ART UNIT	PAPER NUMBER
1633	11

DATE MAILED: 01/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/788 552	BRAUN SERGE
Examiner	**Art Unit**
Beena Puri	1633

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☒ Interview Summary (PTO-413) Paper No(s). *11*
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other

DETAILED ACTION

1. This application claims benefit of 60/246.089 filed on 11/07/2000.

2. In response to a telephonic communication held on Dec. 28 2001, preliminary amendment faxed on Dec. 28 2001 is acknowledged. Claims 2-23 are cancelled and replaced with 24-45 new claims.

3. ***Specification***

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

There are hyperlinks in the specifications (e.g. Page 16). They must be deleted from the specification.

4. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim(s) 24-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected. to make and/or use the invention.

Claims 24, 36-45 are drawn to a method for the treatment of an immune disease comprising administering an effective amount of a nucleic acid capable of expressing beta-interferon to a patient in need of such treatment. Claims 25-35 are drawn to a pharmaceutical composition of a nucleic acid capable of expressing beta-interferon for the treatment of an immune disease.

The following factors have been determined by the courts to be critical in determining whether a claimed invention is enabled (See In re Wands 8 USPQ 2d 1400, Fed. Cir. 1988).

The nature of the invention: The nature of the invention is the use of a nucleic acid that expresses beta interferon for an effective treatment of an immune disease. Thus, the invention falls into the realm of gene therapy.

The state of the prior art and the predictability or unpredictability of the art: The state of the art of gene therapy is in it's infancy and plagued by unpredictability. Clinical efficacy has not been achieved in any gene therapy protocol to date. The following references have been cited herein to illustrate the state of the art of gene therapy. **Martino et al.,** (2000) teaches: "Cytokine therapy in immune-mediated demyelinating diseases of central nervous system: a novel gene therapy approach" (See Title page 184). Martino indicates: "Multiple sclerosis is a chronic disease in which a more persistent therapeutic effect is envisaged. Viral vector technology, although promising, has, therefore, to be improved. Morever, although we obtained consistent results using IL-4 in mice we are aware that the choice for the cytokine to be delivered in human is a very challenging issue" (See page 189, column 1). **Hernberg** (1999)

recites in a review article: "To enable further development of immunotherapy we need to know more about the mechanisms involved in host defense, especially when the system is influenced by extrinsic factors, that is immunomodulative agents" (See abstract, pg. 145). He further indicates: "The mechanisms that regulate the host defense systems are complex, and the influence of extrinsic factors such as immunotherapeutic agents is poorly understood." (See abstract, pg. 145). **Crystal** (1995) recited: "Humans are not simply large mice. There have been several surprise examples, in which predictions from gene transfer studies in experimental animals have not been borne out in human safety and efficacy trials. (Page 409, "What are the obstacles to successful human gene transfer paragraph"). **Anderson** states (1998). "There is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of human diseases (see page 25, column 1, paragraph 1)." Anderson recites: "Gene therapy is a powerful technology that still requires several years before it will make a noticeable impact on the treatment of diseases; Low efficiency of gene transfer and expression in human patients is that we lack a basic understanding of how vectors should be constructed, what regulatory sequences are appropriate for which cell type, how in vivo immune defenses can be overcome" (See page 30, column 1).

All these references refer to the possibility of gene therapy. This is far from enablement and applications. The specification does not provide the skilled artisan with the teachings necessary to overcome the outstanding problems in this respect of gene therapy.

The breadth of the claims and the amount of direction or guidance presented in the specification and the presence or absence of working examples:

As such, the disclosed claims are very broad because the claims are drawn to a method and pharmaceutical composition for the treatment of an immune disease in a patient. The specification (example 1on page 18) teaches the construction of a plasmid construct (pTG13102) which contains human beta interferon expressing gene in the backbone of plasmid pTG11022. The specification further teaches the expression of pTG13102 construct in the mouse myoblast cell line. The specification teaches that biological activity of beta interferon released in the cell culture supernatant is analyzed by its antiviral activity for VSV viruses (example 1, Fig. 1, Table 1, pages 18-20). Furthermore the specification teaches the expression of pTG13102 in 6-8 week old C57B1/10 and SCID mice (Page 20) where mice are treated with notexine to induce muscle regeneration. The specification illustrates that beta interferon is detected in the muscles and sera of both C57B1/10 and SCID mice (Fig. 2A & 2B and Table II on Page 22). These experiments show that nucleic acid construct (pTG13102) is capable of expressing beta interferon in the muscles and released in the blood of the treated mice. However, there are no specific teachings in the specifications that would provide the artisan with any treatment regime to achieve such an effect in humans. Without an art recognized nexus between the disclosed results in the mouse models and the results which the skilled artisan would reasonably expect to observe in humans, the significance of applicant's experimental data is difficult or impossible to interpret. The specification does not address any secretory signal sequence (claim 34 & 44) and

transfecting facilitating vehicle (claim 32 & 42) that could be used in an expression vector to reach a therapeutic level of beta interferon expression in human patients. In addition, there is no correlation between vectors, routes of delivery, that is direct, im, iv, and dosage amounts/frequencies, and the disclose purpose of treatment for multiple sclerosis (claim 28 & 38) or any of the immune diseases recited in the specification (on Page 1). Without guidance from the specification or the prior art, empirical experimentation would be required to determine an effective amount to prevent and treat any immune disease using the said method and pharmaceutical composition.

The quantity of experimentation: To attempt to practice the claimed invention, one of skill in the art would turn to the specification for guidance in practicing the invention. As set forth above, however, the specification lacks sufficient guidance to surmount the technical difficulties recognized in the art. Another source of guidance for one skilled in the art, the prior art, again for reasons set forth above, also lacks solutions to overcome the considerable list of obstacles recognized in the field. In the absence of guidance from the specification and the prior art, one of skilled in the art would resort to experimentation to navigate the obstacles to practicing the claimed invention. Again, as established above, solutions to these technical problems have been elusive despite an enormous amount of experimentation due to a number of factors, including the unpredictable nature of the art. Such unpredictability would warrant even more experimentation, with no true expectation of a measure of success. The amount of experimentation required to practice the claimed invention embodiments would necessitate undue experimentation on the part of one skilled in the art.

In conclusion, given the nature of the invention, the state of the art, the lack of predictability found in the art, the breadth of the claims, the amount of guidance set forth in the specification, and the working example set forth it is concluded that the amount of experimentation necessary to practice necessary to practice the invention is very high and is in fact undue.

5. No claims are allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Beena Puri, Ph. D. whose telephone number is (703)-306-0284. The examiner can normally be reached on 8:00 a. m. EST. to 4:30 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark can be reached on (703)-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are (703)-308-4242 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)-308-0196.

Beena Puri, Ph. D.
Patent Examiner
AU1633
Jan. 7, 2002.

PRIMARY EXAMINER